

CLAIMS

1. A method for the non-invasive determination of the concentration of a substance (glucose) in blood of a subject, the method comprising the steps of:

(a) placing an electrical conducting probe against a skin surface of the subject, wherein the probe comprises a plurality of electrodes, each electrode comprising a spike, the spikes being laterally spaced apart from each other and being of sufficient length to penetrate the stratum corneum;

(b) passing an electrical current through the electrodes to obtain a value of impedance for the skin; and

(c) converting the impedance to said concentration.

2. A method according to claim 1, wherein each spike is at least 10 μm in length.

3. The method of claim 1 or claim 2, wherein the probe comprises three said electrodes, the spikes of first and second of the electrodes being laterally spaced a first distance from each other, the spikes of the first and third electrodes being laterally spaced a second distance from each other, and wherein and step (b) includes separately passing an electrical current between the first and second electrodes and the first and third electrodes to obtain first and second said values of skin impedance.

4. The method of claim 3, wherein the first and second distances are different from each other.

5. The method of claim 3 or 4, wherein the first distance is between about 0.1mm and about 40 mm; or between about 0.1 mm and 30 mm; or between about 0.1 mm and 25 mm; or between about 0.1 mm and 20 mm; or between about 0.1 mm and 15 mm; or between about 0.2 mm and 10 mm; or between about 0.2 mm and 8 mm; or between about 0.2 mm and 5 mm; or between about 0.2 mm and 3 mm; or between about 0.2 mm and 2 mm; or between about 0.2 mm and 1.5 mm; or between about 0.2 mm and 1 mm; or between about 0.2 mm and 0.5 mm.

6. The method of claim 5, wherein the second distance is between about 1 mm and about 50 mm; or between about 1 mm and 40 mm; or between about 1 mm and 30 mm; or between about 1 mm and 25 mm; or between about 1 mm and 20 mm; or between about 1 mm and 15 mm; or between about 1 mm and 10 mm; or between about 1 mm and 9 mm; or between about 1 mm and 8 mm; or between about 1 mm and 7 mm; or between about 2 mm and 8 mm; or between about 3 mm and 7 mm; or between about 4 mm and 7 mm; or between about 4 mm and 6 mm; or about 5 mm.

7. The method of any preceding claim, wherein for each electrode, there are at least two said spikes, or at least three said spikes, or at least four said spikes, or at least five said spikes, or at least six said spikes, or at least seven said spikes, or at least eight said spikes, or at least nine said spikes, or at least ten said spikes, or at least twelve said spikes, or at least fifteen said spikes, or at least eighteen said spikes, or at least twenty said spikes, or at least twenty-five said spikes, or at least thirty said spikes, or at least thirty-five said spikes, or at least fifty said spikes.

8. The method of any preceding claim wherein each said spike is up to 250, or up to 240, or up to 230, or up to 220, or up to 210, or up to 200, or up to 190 or up to 180 or up to 170 or up to 160 or up to 150 or up to 140 or up to 130 or up to 120 or up to 110 or up to 100 μm in length.

9. The method of any preceding claim wherein each said spike is at least 20, or at least 30 or at least 40 or at least 50, or at least 60 or is at least 70 or is at least 80 or is at least 90 μm in length.

10. The method of any preceding claim, wherein each said spike is of sufficient length to penetrate below the skin surface to the *Stratum Germinativum*.

11. The method of any preceding claim, wherein the outer diameter of each spike on the electrodes is between about 20 μm and about 50 μm .

12. The method of any preceding claim, wherein said electrical current has a frequency of between about 10 Hz and about 10 MHz.

13. The method of claim 12, wherein step (b) is conducted a first time at a first said frequency, and step (b) is conducted a second time at a second said frequency.

14. A method for diagnosing a diseased condition of the skin, the method comprising the steps of:

- (i) placing an electrical conducting probe against a skin surface of the subject, wherein the probe comprises a plurality of electrodes, each electrode furnished with a number of spikes, the spikes being laterally spaced apart from each other and being of sufficient length to penetrate the stratum corneum;
- (ii) passing an electrical current through the electrodes to obtain a value of skin impedance; and
- (iii) using reference data to determine whether the impedance value indicates the diseased condition.

15. The method of claim 14, wherein the diseased condition is cancer, preferably skin cancer.

16. The method of claim 15, wherein said skin cancer is a basal cell sarcoma, a malignant melanoma, a squamous cell carcinoma, or precursors of such lesions.

17. A method according to any of claims 14 to 16, wherein each spike is at least 10 μm in length.

18. The method of any of claims 14 to 17, wherein the probe comprises three said spike furnished electrodes, the first and second electrodes being laterally spaced a first distance from each other, the spikes of the first and third electrodes being laterally spaced a second distance from each other, and wherein and step (b) includes separately passing an electrical current between the first and second electrodes and the first and third electrodes to obtain first and second said values of skin impedance.

19. The method of claim 18, wherein the first and second distances are different from each other.

20. The method of claim 18 or 19, wherein the first distance is between about 0.1 mm and about 40 mm; or between about 0.1 mm and 30 mm; or between about 0.1 mm and 25 mm; or between about 0.1 mm and 20 mm; or between about 0.1 mm and 15 mm; or between about 0.2 mm and 10 mm; or between about 0.2 mm and 8 mm; or between about 0.2 mm and 5 mm; or between about 0.2 mm and 3 mm; or between about 0.2 mm and 2 mm; or between about 0.2 mm and 1.5 mm; or between about 0.2 mm and 1 mm; or between about 0.2 mm and 0.5 mm.

21. The method of claim 20, wherein the second distance is between about 1 mm and about 50 mm; or between about 1 mm and 40 mm; or between about 1 mm and 30 mm; or between about 1 mm and 25 mm; or between about 1 mm and 20 mm; or between about 1 mm and 15 mm; or between about 1 mm and 10 mm; or between about 1 mm and 9 mm; or between about 1 mm and 8 mm; or between about 1 mm and 7 mm; or between about 2 mm and 8 mm; or between about 3 mm and 7 mm; or between about 4 mm and 7 mm; or between about 4 mm and 6 mm; or about 5 mm.

22. The method of any of claims 14 to 21, wherein for each electrode, there are at least two said spikes, or at least three said spikes, or at least four said spikes, or at least five said spikes, or at least six said spikes, or at least seven said spikes, or at least eight said spikes, or at least nine said spikes, or at least ten said spikes, or at least twelve said spikes, or at least fifteen said spikes, or at eighteen said spikes, or at least twenty said spikes, or at least twenty-five said spikes, or at least thirty said spikes, or at least thirty-five said spikes, or at least fifty said spikes.

23. The method of any of claims 14 to 22 wherein each said spike is up to 250, or up to 240, or up to 230, or up to 220, or up to 210, or up to 200, or up to 190 or up to 180 or up to 170 or up to 160 or up to 150 or up to 140 or up to 130 or up to 120 or up to 110 or up to 100 μ m in length.

24. The method of any of claims 14 to 23 wherein each said spike is at least 20, or at least 30 or at least 40 or at least 50, or at least 60 or is at least 70 or is at least 80 or is at least 90 μm in length.

5 25. The method of any of claims 14 to 24, wherein each said spike is of sufficient length to penetrate below the skin surface to the *Stratum Germinativum* or through the *Stratum Corneum* into the living *Epidermis* but not into the *Dermis*.

10 26. The method of any of claims 14 to 26, wherein the outer diameter of each spike is between about 20 μm and about 50 μm .

27. The method of any of claims 14 to 26, wherein said electrical current has a frequency of between about 10 Hz and about 10 MHz.

15 28. The method of claim 27, wherein step (b) is conducted a first time at a first said frequency, and step (b) is conducted a second time at a second said frequency.

20 29. The method of any one of claims 14 to 16, wherein both non-invasive surface electrodes (conventional probes) are used in conjunction with said minimally invasive spiked electrodes to catch more aspects of skin properties in order to improve power of discrimination.